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Case Report

Active pulmonary tuberculosis in a patient with secukinumab treatment☆,☆☆

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ABSTRACT

Numerous investigations have documented active tuberculosis (TB) infection following biologic treatment. One of the most secure biologic medications for infections is secukinumab. Additionally, no cases of active TB while receiving secukinumab therapy were recorded. Secukinumab 150 mg per month has been administered for a 19-year-old man with spondyloarthritis since May 2020. A diagnosis of pulmonary TB was made when the patient complained of a moderate fever, a productive cough, and weight loss after 2 years. His fever and respiratory symptoms were relieved after 6 weeks of treatment by stopping secukinumab and utilizing 4 antibiotics: isoniazid, rifampicin, pyrazinamide, and ethambutol, while nonsteroidal anti-inflammatory drugs reduced his joint and back discomfort. During biological therapy, even with secukinumab, annual screening for latent and active TB is crucial. We require additional study on secukinumab-treated patients with active TB in nations with high TB burdens, including Vietnam.

Introduction

Spondyloarthritis is a chronic inflammatory arthritis condition that affects the joints and extra-articular organs, causing spinal stiffness, peripheral joint destruction, and organ damage, including to the eyes and intestines, reducing quality of life. Biological therapeutic agents are highly effective in controlling the symptoms of spondyloarthritis and slowing disease progression. Secukinumab, a fully human monoclonal antibody directed against interleukin (IL)-17A, was approved by the Food and Drug Administration for the treatment of ankylosing spondylitis in 2015 [1]. Secukinumab has also been

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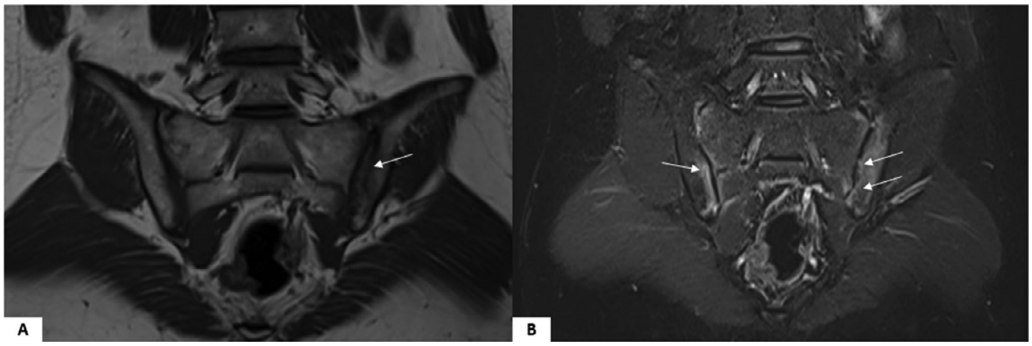

Fig. 1. – Magnetic resonance imaging of the sacroiliac joint. (A) Bone marrow edema appears as a hypointense signal on T1-weighted images. (B) Bone marrow edema appears as a hyperintense signal on short tau inversion recovery images.

shown to be effective in patients with radiographic and non-radiographic axial spondyloarthritis [2–5].

However, the use of biological therapeutic agents can increase the risk of infections, such as TB caused by *Mycobacterium tuberculosis*, which is the leading cause of infection agent-related death. More than 1.5 million deaths are estimated to be caused by TB [6]. Vietnam is considered to have a high burden of TB, and new TB infections in 2018 were identified in approximately 174,000 people, with deaths reported in 12,000 cases [7]. Most cases were diagnosed as pulmonary TB, increasing the risk of transmission and the burden of disease. Many studies have shown that anti-tumor necrosis factor (TNF) therapy is associated with TB outbreaks, including cases of patients with spondyloarthritis who were diagnosed with TB while undergoing TNF treatment [8–11]. Secukinumab has a good long-term safety profile, with no cases of active TB reported during therapy to date [12–15]. We report the first case of active pulmonary TB in a patient being treated with secukinumab.

Case report

A 19-year-old man presented with peripheral spondyloarthritis characterized by typical magnetic resonance imaging (Fig. 1). The patient was prescribed 150 mg secukinumab monthly starting in May 2020 after a poor response to sulfasalazine and non-steroidal anti-inflammatory drugs. Before receiving biologic therapy, the patient was screened for latent TB and was found to have a negative QuantiFERON-TB test and a normal chest X-ray. The patient had a good response to secukinumab, and musculoskeletal symptoms improved significantly after several months of treatment.

In April 2022, the patient complained of fatigue, mild fever, productive cough, and weight loss lasting for 2 weeks. Physical examination revealed crackle rales in the left lung and no abnormalities in any other organs. Laboratory results demonstrated an elevated C-reactive protein level of 44 mg/dL and an erythrocyte sedimentation rate of 75 mm. Other hematological and biochemical tests, such as complete blood count, liver enzymes, renal function, glycemia, and thyroid function, were normal. The patient tested negative for human immunedeficiency virus, hepatitis B virus, and hepatitis C virus. Chest X-ray showed left upper lobe consolidation (Fig. 2), and a bronchoalveolar lavage test indicated a negative acid-fast Bacilli smear and detected *M tuberculosis*, which was found to be sensitive to rifampicin and isoniazid by a line probe assay. Bronchoscopic biopsy demonstrated caseating granulomatous inflammation (Fig. 3).

The patient was diagnosed with active pulmonary TB. The initial treatment for TB was 4 antibiotics: isoniazid, rifampicin, pyrazinamide, and ethambutol. Secukinumab was discontinued due to concerns regarding the reactivation of latent TB. Joint pain and back pain were eased by high doses of non-steroidal anti-inflammatory drugs. After 8 weeks of anti-TB treatment, the patient's fever and respiratory symptoms resolved, and the lesion on the chest X-ray improved. Joint pain and back pain were mostly controlled.

Discussion

The cell-mediated immune pathway is fundamental in generating the body's defenses against infection, with interferon production playing a crucial role in controlling bacterial proliferation, including *M tuberculosis*, the causative agent for TB [16]. Although the mechanism involved in the increased risk of TB infection when undergoing biological anti-TNF therapy is understood [17], the role of IL-17 in TB pathogenesis remains controversial. Several studies have shown that IL-17 plays a protective role against TB infection, acting as a modulator of the inflammatory response [18].

In an IL-123 p19–deficient mouse model, the number of IFN-producing, antigen-specific CD4 T cells did not decrease, even after most IL-17–producing CD4 T cells were lost [19]. These data support the hypothesis that the depletion of IL-17–producing CD4 T cells is unrelated to the progression of *M tuberculosis*. In a meta-analysis of 28 clinical trials, including 12,319 patients with spondyloarthropathy who received an average of 5 years of secukinumab treatment, only 7 patients were diagnosed with latent TB infections, and no cases of active TB were reported. Notably, most trials included in this meta-analysis were conducted in developing countries where the prevalence of TB is low [20].

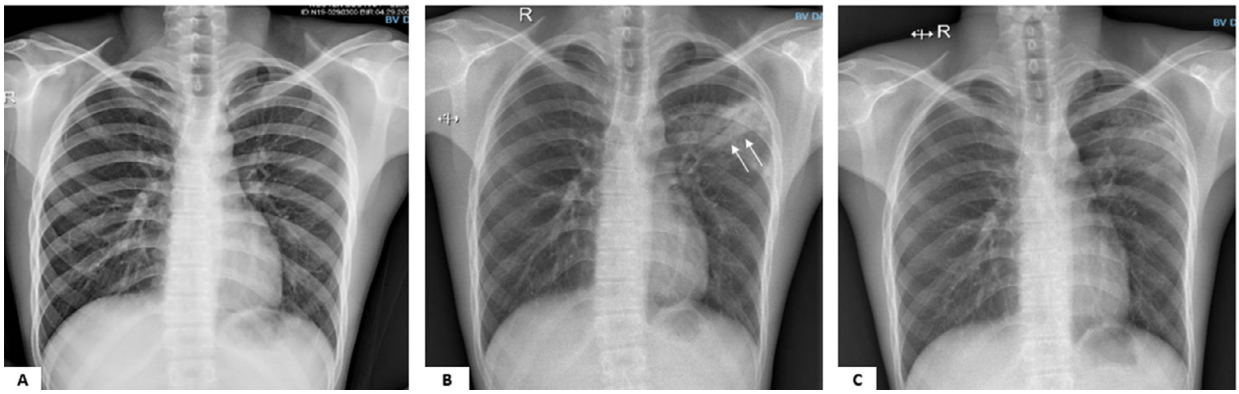

Fig. 2. – Chest X-ray. (A) Normal chest X-ray before secukinumab treatment. (B) Chest X-ray performed after 2 years of secukinumab therapy showed consolidation in the left upper lobe (long white arrows). (C) Chest X-ray after 4 months of anti-TB therapy showed that consolidation was reduced significantly.

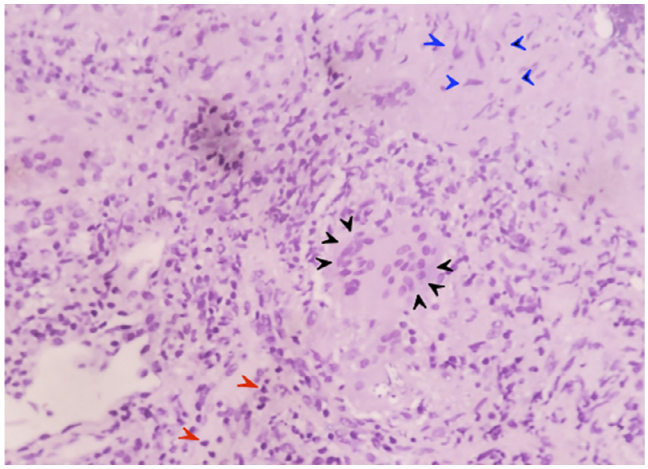

Fig. 3. – Histologic examination of a bronchoscopic biopsy sample (hematoxylin and eosin), showing granulomatous inflammation (black arrows: giant cells; blue arrows: histiocytes; red arrows: lymphocytes).

Biologic-naive patients with spondyloarthritis do not have a significantly increased TB risk compared with the general population [20]. In this case, aside from the use of biologic drugs, the patient had no additional risk factors for TB, such as the long-term use of corticosteroids, frailty, immunodeficiency diseases (eg, human immune-deficiency virus), or latent TB. Screening for latent TB is intended to detect and treat endogenous *M tuberculosis* infections to prevent the progression to active TB. However, patients are at a high risk of exogenous *M tuberculosis* infections for the duration of biological treatments, especially in high TB burden countries, such as Vietnam. Unfortunately, this patient was not screened for latent TB annually during the 2 years of biologic therapy.

Whether the risk of new TB infections increases when using secukinumab remains inconclusive, as this is the only case reported of a patient developing TB while receiving secukinumab. However, this is the first report of an active TB diagnosis during secukinumab treatment in a patient that was previously free of either latent or active pulmonary TB.

This case report demonstrates that both before and during biologic therapy, even with secukinumab, patients should be screened for latent *M tuberculosis* infections annually, even if previous tests were negative, to facilitate the early detection of such infections and allow for prompt treatment before progression to active TB [21]. TB prophylaxis with isoniazid alone or isoniazid combined with rifampicin is recommended for patients who have positive tests for latent infections. Increased attention to clinical symptoms, such as fatigue, fever, prolonged cough, and weight loss, can also be used to monitor for active pulmonary TB. Chest X-rays should be performed yearly to screen for the early stages of active pulmonary TB, even before symptom onset.

Conclusion

In countries with a high TB burden, patients receiving biologic treatments should be screened for TB annually. Both latent and active TB should be monitored to provide appropriate treatment to resolve TB sequelae, reducing morbidity and mortality from the disease. Additional research regarding active TB in patients treated with secukinumab remains necessary, particularly in high-burden TB countries such as Vietnam, to clarify the risk of TB in these patients.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Authors' contributions

Cao TN and Nguyen MD contributed equally to this article as co-first authors. All authors read and approved final version of this manuscript.

Ethics approval

Not applicable.

Patient consent

Written informed consent was obtained from the patient for the publication of patient information in this article.

REFERENCES

[1] Blair HA. Secukinumab: a review in ankylosing spondylitis. Drugs 2019;79(4):433–43. doi:10.1007/s40265-019-01075-3.

[2] Kivitz AJ, Wagner U, Dokoupilova E, Supronik J, Martin R, Talloczy Z, et al. Efficacy and safety of secukinumab 150 mg with and without loading regimen in ankylosing spondylitis: 104-week results from MEASURE 4 study. Rheumatol Ther 2018;5(2):447–62. doi:10.1007/s40744-018-0123-5.

[3] Baraliakos X, Braun J, Deodhar A, Poddubnyy D, Kivitz A, Tahir H, et al. Long-term efficacy and safety of secukinumab 150 mg in ankylosing spondylitis: 5-year results from the phase III MEASURE 1 extension study. RMD Open 2019;5(2):e001005.

[4] Poddubnyy D, Deodhar A, Baraliakos X, Blanco R, Dokoupilova E, Hall S, et al. POS0900 secukinumab 150 mg provides sustained improvement in signs and symptoms of non-radiographic axial spondyloarthritis: 2-year results from the PREVENT study. Ann Rheum Dis 2021;80:707.

[5] Baeten D, Baraliakos X, Braun J, Sieper J, Emery P, van der Heijde D, et al. Anti-interleukin-17A monoclonal antibody secukinumab in treatment of ankylosing spondylitis: a randomised, double-blind, placebo-controlled trial. Lancet 2013;382(9906):1705–13. doi:10.1016/S0140-6736(13)61134-4.

[6] Chakaya J, Khan M, Ntoumi F, Aklillu E, Fatima R, Mwaba P, et al. Global tuberculosis report 2020—reflections on the global TB burden, treatment and prevention efforts. Int J Infect Dis 2021;113(suppl 1):S7–S12. doi:10.1016/j.ijid.2021.02.107.

[7] World Health Organization. Global action plan on physical activity 2018-2030: more active people for a healthier world 2019.

[8] Jauregui-Amezaga A, Turon F, Ordás I, Gallego M, Feu F, Ricart E, et al. Risk of developing tuberculosis under anti-TNF treatment despite latent infection screening. J Crohns Colitis 2013;7(3):208–12. doi:10.1016/j.crohns.2012.05.012.

[9] Zhang Z, Fan W, Yang G, Xu Z, Wang J, Cheng Q, et al. Risk of tuberculosis in patients treated with TNF-α antagonists: a systematic review and meta-analysis of randomised controlled trials. BMJ Open 2017;7(3):e012567. doi:10.1136/bmjopen-2016-012567.

[10] Sartori N, Andrade N, Chakr R. AB1231 Incidence of tuberculosis in patients with rheumatic diseases using TNF inhibitors: a systematic review. Ann Rheum Dis 2019;78:2077–8.

[11] Snast I, Bercovici E, Solomon-Cohen E, Avni T, Shitenberg D, Hodak E, et al. Active tuberculosis in patients with psoriasis receiving biologic therapy: a systematic review. Am J Clin Dermatol 2019;20(4):483–91. doi:10.1007/s40257-019-00432-y.

[12] Elewski BE, Baddley JW, Deodhar AA, Magrey M, Rich PA, Soriano ER, et al. Association of secukinumab treatment with tuberculosis reactivation in patients with psoriasis, psoriatic arthritis, or ankylosing spondylitis. JAMA Dermatol 2021;157(1):43–51 Erratum in: JAMA Dermatol. 2021 Jan 1;157(1):124. PMID: 33001147; PMCID: PMC7527940. doi:10.1001/jamadermatol.2020.3257.

[13] Kammüller M, Tsai TF, Griffiths CE, Kapoor N, Kolattukudy PE, Brees D, et al. Inhibition of IL-17A by secukinumab shows no evidence of increased *Mycobacterium tuberculosis* infections. Clin Transl Immunol 2017;6(8):e152. doi:10.1038/cti.2017.34.

[14] van de Kerkhof PC, Griffiths CE, Reich K, Leonardi CL, Blauvelt A, Tsai TF, et al. Secukinumab long-term safety experience: a pooled analysis of 10 phase II and III clinical studies in patients with moderate to severe plaque psoriasis. J Am Acad Dermatol 2016;75(1):83–98 .e4. doi:10.1016/j.jaad.2016.03.024.

[15] Fowler E, Ghamrawi RI, Ghiam N, Liao W, Wu JJ. Risk of tuberculosis reactivation during interleukin-17 inhibitor therapy for psoriasis: a systematic review. J Eur Acad Dermatol Venereol 2020;34(7):1449–56. doi:10.1111/jdv.16254.

[16] Snyder DT, Hedges JF, Jutila MA. Getting "inside" type I IFNs: type I IFNs in intracellular bacterial infections. J Immunol Res 2017;2017:9361802. doi:10.1155/2017/9361802.

[17] Keane J, Gershon S, Wise RP, Mirabile-Levens E, Kasznica J, Schwieterman WD, et al. Tuberculosis associated with infliximab, a tumor necrosis factor alpha-neutralizing agent. N Engl J Med 2001;345(15):1098–104. doi:10.1056/NEJMoa011110.

[18] Khader SA, Cooper AM. IL-23 and IL-17 in tuberculosis. Cytokine 2008;41(2):79–83. doi:10.1016/j.cyto.2007.11.022.

[19] Khader SA, Pearl JE, Sakamoto K, Gilmartin L, Bell GK, Jelley-Gibbs DM, et al. IL-23 compensates for the absence of IL-12p70 and is essential for the IL-17 response during tuberculosis but is dispensable for protection and antigen-specific IFN-gamma responses if IL-12p70 is available. J Immunol 2005;175(2):788–95. doi:10.4049/jimmunol.175.2.788.

[20] Gottlieb AB, Deodhar A, Mcinnes IB, Baraliakos X, Reich K, Schreiber S, et al. Long-term safety of secukinumab over five years in patients with moderate-to-severe plaque psoriasis, psoriatic arthritis and ankylosing spondylitis: update on integrated pooled clinical trial and post-marketing surveillance data. Acta Derm Venereol 2022;102:adv00698.

[21] O'Young CKY, Ho KM, So H, Mok TYW, Leung CC, Chau CH, et al. Recommendations on management of latent tuberculosis infection in patients initiating anti-tumor necrosis factor biologics. J Clin Rheumatol Immunol 2021;21(02):51–7.